

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of the claims in the application:

Listing of Claims:

1 - 134. (Cancelled).

135. (New) A method of predicting the receptor-modulating activity of a test compound when bound to a receptor, comprising the steps of:

(1) (a) providing a receptor;

(b) contacting said receptor with a plurality of reference compounds, said reference compounds known to modulate the biological activity of said receptor, and wherein the binding of each reference compound to said receptor forms a reference conformation;

(c) providing a panel comprising a plurality of members, wherein said members of said panel possess differential ability to bind to said reference conformation;

(d) contacting said reference conformation with said panel;

(e) measuring the effect of said reference compound on the binding of said panel members to said receptor, said measuring step forming a fingerprint for each member of said plurality of reference compounds;

(2) (a) providing a test compound;

(b) contacting said receptor with said test compound, wherein the binding of said test compound to said receptor forms a test conformation;

(c) contacting said test conformation with said panel;

(d) measuring the effect of said test compound on the binding of said panel member; and

(3) comparing the effect of said test compound on the binding of said panel member to said fingerprints to predict the receptor-modulating activity of said test substance when bound to said receptor.

136. (New) The method of claim 135, wherein said fingerprint for each member of said plurality of reference compounds comprises a plurality of panel-based descriptors, each panel-based descriptor characterizing the effect of said reference compound on the binding of a particular panel member to said receptor, said panel-based descriptors collectively characterizing the effect of said reference compound on the binding of all of the panel members, individually, to said receptor.

137. (New) The method of claim 136, wherein said panel members are obtained by a method which comprises:

(a) providing at least one ligand for the receptor;

(b) screening a first combinatorial library comprising a plurality of members for the ability to bind to a receptor in at least two different reference conformations, including at least one ligand-bound conformation, and

(c) based on said screening, providing a panel of first library members, said panel comprising members which differ with

respect to their ability to binding to the receptor, depending on its conformation.

138. (New) The method of claim 137, wherein a plurality of different ligands are used.

139. (New) The method of claim 135, wherein said biological activity of said reference compounds at said receptor is known for a plurality of different tissues, so that the biological activity of said test compound in said tissues is predicted.

140. (New) The method of claim 135, wherein said receptor is a nuclear receptor.

141. (New) The method of claim 135, wherein said receptor is an estrogen receptor (ER).

142. (New) The method of claim 135, wherein said reference compound is a pharmacological agonist or antagonist of said receptor.

143. (New) The method of claim 137, wherein said first combinatorial library is an oligopeptide library.

144. (New) The method of claim 135, wherein said test compounds are provided and screened in the form of a combinatorial library.

145. (New) The method of claim 135, wherein said test compound comprises an organic compound with a molecular weight of less than 500 daltons.

146. (New) The method of claim 135, wherein said contacting steps are performed in vitro.

147. (New) The method of claim 141, wherein at least one reference compound is selected from the group consisting of estradiol, estriol, nafoxidine, 4-OH tamoxifen, clomifene, premarin, raloxifene, ICI 182, 780, 16 α -OH estrone, and progesterone.

148. (New) The method of claim 140, wherein at least one panel member is a peptide comprising Leu-Xaa-Xaa-Leu-Leu.

149. (New) The method of claim 141, wherein at least one panel member has a substantially higher affinity for ER α than for ER β , and at least one other panel member has a substantially higher affinity for ER β than for ER α .

150. (New) The method of claim 141, wherein at least one panel member binds the receptor substantially more strongly when the receptor is bound to estradiol than when the receptor is not so bound.

151. The method of claim 141, wherein at least one panel member binds the receptor substantially less strongly when the receptor is bound to estradiol when it is not so bound.

152. The method of claim 141, wherein said panel comprises:

(1) at least one member with a substantially higher affinity for ER β than for ER α , whose affinity is substantially greater for estradiol-bound ER than for unliganded ER;

(2) at least one member with a substantially higher affinity for ER α than for ER β , whose affinity is substantially the same for estradiol-bound ER and for unliganded ER;

(3) at least one member with a substantially higher affinity for ER α than for ER β , whose affinity is higher for estradiol-bound ER α than for unliganded ER α , and substantially the same for estradiol-bound ER β and unliganded ER β ;

(4) at least one member with a higher affinity for ER α than for ER β , whose affinity is substantially lower for estradiol bound ER α than for unliganded ER α , and substantially the same for estradiol-bound ER β and unliganded ER β ; and

(5) at least one member with a substantially higher affinity for ER β than for ER α , and whose affinity is substantially lower for estradiol-bound ER than for unliganded ER.

153. (New) The method of claim 141, wherein said reference conformations include a plurality of conformations selected from the group consisting of unliganded receptor, estradiol-liganded receptor, 4-OH tamoxifen liganded receptor, estriol-liganded receptor, nafoxidene-liganded receptor, clomifene-liganded receptor, premarin-liganded receptor, raloxifene-liganded receptor, ICI 182, 780-liganded receptor, 16 α -OH estrone-liganded receptor, and progesterone-liganded receptor.

154. (New) The method of claim 141, wherein said panel comprises members representing a plurality of classes selected from the group consisting of ER α / β I, ER α / β II, ER α / β III, ER α / β IV, ER α I, ER α II, ER α III, ER β I, ER β II, and ER β III.

155. (New) The method of claim 141, wherein said method distinguishes among 4-OH tamoxifen, nafoxidene, clomiphene, and ratoxifene.

156. (New) The method of claim 135, wherein said conformations comprise a first liganded conformation induced by a first ligand and a second liganded conformation induced by a second and different ligand.

157. (New) The method of claim 140, wherein at least one member of said panel is a Table 10 peptide, α/β I, α/β II, α/β III, α/β IV, α/β V, α I, α II, α III, β I, β II, and β III, or peptides having the same characterizing binding activity against reference conformations of ER, and markedly identical to at least one of said Table 10 peptides.